

WHAT IS CLAIMED IS:

1. A purified and isolated polypeptide having the primary structural conformation and biological properties of naturally-occurring metalloproteinase inhibitor.
2. A polypeptide according to Claim 1 wherein said polypeptide is the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.
3. A polypeptide according to Claim 1 further characterized by being free of association with any mammalian protein.
4. A polypeptide according to Claim 2 wherein the exogenous DNA sequence is a cDNA sequence.
5. A polypeptide according to Claim 2 wherein the polypeptide is bovine metalloproteinase inhibitor.
6. A polypeptide according to Claim 2 wherein the exogenous DNA sequence is a genomic DNA sequence.
7. A polypeptide according to Claim 2 wherein the exogenous DNA sequence is carried on an autonomously replicating DNA plasmid or viral vector.
8. A polypeptide according to Claim 1 possessing part or all of the primary structural conformation of human metalloproteinase inhibitor as set forth in Figure 2 or any naturally occurring allelic variant thereof.

9. A polypeptide according to Claim 1 which has the immunological properties of naturally-occurring metalloproteinase inhibitor.

5 10. A polypeptide according to Claim 1 which has the in vitro biological activity of naturally-occurring metalloproteinase inhibitor.

10 11. A polypeptide according to Claim 1 further characterized by being covalently associated with a detectable label substance.

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15 12. A DNA sequence for use in securing expression in a procaryotic or eucaryotic host cell of a polypeptide product having at least a part of the primary structural conformation and one or more of the biological properties of naturally-occurring metalloproteinase inhibitor, said DNA sequence selected from among:

20 (a) the DNA sequence set out in Figure 1 or Figure 2 or their complementary strands;

 (b) DNA sequences which hybridize to the DNA sequences defined in (a) or fragments thereof; and

25 (c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).

30 13. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to Claim 12 in a manner allowing the host cell to express said polypeptide product.

35 14. A polypeptide product of the expression of a DNA sequence of Claim 12 in a procaryotic or eucaryotic host.

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15. A purified and isolated DNA sequence coding for procaryotic or eucaryotic host expression of a polypeptide having the primary structural conformation and biological properties of metalloproteinase inhibitor.

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16. A cDNA sequence according to Claim 15.

17. A genomic DNA sequence according to Claim 15.

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18. A DNA sequence according to Claim 15 wherein said DNA sequence codes for human metalloproteinase inhibitor.

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19. A DNA sequence according to Claim 18 and including one or more codons preferred for expression in E. coli cells.

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20. A DNA sequence according to Claim 15 having the sequence set out in Figure 2.

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21. A DNA sequence according to Claim 15 and including one or more codons preferred for expression in yeast cells.

22. A DNA sequence according to Claim 15 covalently associated with a detectable label substance.

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23. A DNA sequence coding for a polypeptide fragment or polypeptide analog of naturally-occurring metalloproteinase inhibitor.

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24. A DNA sequence as in Claim 23 coding for methionyl metalloproteinase inhibitor.

25. A biologically functional plasmid or viral DNA vector including a DNA sequence according to Claim 12.

5 26. A procaryotic or eucaryotic host cell stably transformed or transfected with a DNA vector according to Claim 25.

10 27. A polypeptide product of the expression in a procaryotic or eucaryotic host cell of a DNA sequence according to Claim 15.

15 28. A synthetic polypeptide having part or all of the amino acid sequence as set forth in Figure 2 and having one or more of the in vitro biological activities of naturally-occurring metalloproteinase inhibitor.

20 29. A synthetic polypeptide having part or all of the secondary conformation of part or all of the amino acid sequence set forth in Figure 2 and having a biological property of naturally-occurring human metalloproteinase inhibitor.

25 30. A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological properties of naturally occurring metalloproteinase inhibitor, said process comprising:

30 growing, under suitable nutrient conditions, procaryotic or eucaryotic host cells transformed or transfected with a DNA vector according to Claim 25, and isolating desired ^{metalloproteinase inhibitor} polypeptide products of the expression of DNA sequences in said vector.

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31. Purified and isolated human metalloproteinase inhibitor free of association with any human protein in glycosylated or nonglycosylated form. /

5 32. A pharmaceutical composition comprising an effective amount of a polypeptide according to Claim 1 and a pharmaceutically acceptable diluent, adjuvant or carrier.

10 33. A method for inhibiting tumor cell dissemination in a mammal comprising administering an effective amount of a polypeptide according to Claim 1.

15 34. A method for treating rheumatoid arthritis in a mammal comprising administering an effective amount of a polypeptide according to Claim 1.

20 35. A DNA sequence coding for an analog of human metalloproteinase inhibitor selected from the group consisting of:
a) [Met⁻¹] metalloproteinase inhibitor; and
b) metalloproteinase inhibitor wherein one or more cysteines are replaced by alanine or serine. /

25 36. A polypeptide product of the expression in a procaryotic or eucaryotic host cell of a DNA sequence according to Claim 35.

30 37. A preparation of MI which is greater than 95% pure and which comprises less than 0.5 ng of pyrogen per 0.5 mg of metalloproteinase inhibitor.

35 38. An antibody specifically binding metalloproteinase inhibitor.

39. An antibody as in Claim 38 wherein said antibody is a monoclonal antibody.

add
#1

add
#2